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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/555,350 | 08/24/2000 | Klaus Cichutek | 11692-004001 | 3834 |

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| EXAMINER | |
|---|---|
| WINKLER, ULRIKE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | 22 |

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/555,350 | CICHUTEK ET AL. | |
| | Examiner | Art Unit | |
| | Ulrike Winkler | 1648 | |

*-- The MAILING DATE of this c mmunication appears on the c ver sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9 and 19* is/are allowed.

6)☐ Claim(s) *1-8 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

The Amendment filed August 11, 2003 (Paper No. 21) in response to the Office Action of May 6, 2003 is acknowledged and has been entered. Claims 10-18 have been cancelled, claims 19 and 20 have been added. Claims 1-9, 19 and 20 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

### *Specification*

The Office acknowledges the update to the specification indicating the priority.

### *Drawings*

The Office acknowledges that Applicants have supplied drawing, however the drawings have not been matched with the case. Applicant is requested to provide another set of drawing for the case; the Office apologizes for any inconvenience this may have caused Applicant.

### *Claim Rejections - 35 USC § 112*

The rejection of claims 1 and 9 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification is withdrawn in view of applicant's amendment to the claim 9 now reciting SEQ ID NO: 1 instead of the plasmid by name.

***Claim Rejections - 35 USC § 102***

The rejection of claims 1-8 under 35 U.S.C. 102(e) as being anticipated by Dornburg (U.S. Pat No. 5,869,331) as evidenced by Novotny et al. (in Molecular Biology and Biotechnology, 1995) **is withdrawn** in favor of the new 35 U.S.C. 103 rejection below.

New Rejection:

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dornburg (U.S. Pat No. 5,869,331), Novotny et al. (in Molecular Biology and Biotechnology, 1995), Colcher et al. (Journal of the National Cancer Institute, 1990) and June et al. (U.S. Pat. No. 6,352,694 et al.).

The instant invention is drawn to a cell-specific retroviral vector, comprising the steps of making a single chain antibody (steps a-g) against a cell surface receptor (immunizing animal with cell population) the single chain antibody encoding DNA is then inserted into a psi-negative retroviral expression vector. The retroviral Env expression vector is from spleen necrosis virus (SNV).

Dornburg teaches a retroviral vector particles having target cell specificity which comprises a retroviral vector having a targeting peptide fused to the envelope protein of the retroviral vector to form a targeting envelope. The targeting peptide replaces or disrupts the natural viral receptor binding site and the targeting peptide is a peptide that specifically binds a specific receptor of the target cell (see abstract). To alter the host range of a vector particle, retroviral vector particles may be constructed that contain modified envelope proteins that recognize only a cell surface structure (receptor) specific for the target cell of interest. Proteins known to recognize specific structures of proteins are antibody molecules. Hence, to make a retroviral vector particle specific for a cell-type of interest, the viral receptor binding peptide may be replaced with an antigen binding site of an antibody molecule (see column 4, lines 25-34). To construct a targeting envelope containing the antigen binding site of an antibody directed against a cell-surface protein expressed on several human tumor cells, the corresponding single chain antibody gene (termed B6.2) made for expression in *E. coli.* was modified in the following way: PCR technology was used to amplify the B6.2 scA gene using the original *E. coli.* expression plasmid as template (see column 7, lines 31-35). Helper cells are made by the transfection of plasmids expressing all retroviral proteins necessary to form infectious virus particles. One plasmid is designed to express all core/proteins (expression of gag and pol). The other plasmid is designed to express the envelope precursor/protein. Both plasmid constructs do not contain retroviral cis/acting sequences for virus replication (e.g., encapsidation sequences, a primer binding site etc.) (see column 13, lines 5-30). Plasmids expressing mutant envelope genes of spleen necrosis virus (SNV) are used in the process (see column 13, lines 34-50). The production of antibodies to cell surface receptors is well known to require the injection of cells

into an animal. The reference teaches that the envelope constructs can be made to recognize specific receptors of target cells, the reference does not disclose immunizing an animal with a whole cell.

Colcher et al. teaches that the Mab B6.2 IgG, used by Dornburg above, was generated by the immunization of Balb/c mice with membrane-enriched fraction of a human breast tumor (see material and methods). The reference does not teach injecting whole cells into the animal.

Novotny et al. teaches the standard step required for the production of single chain antibodies has become a standard technique in the art. The figure discloses that the rearranged V genes are amplified using PCR, IgG mRNA can be used to obtain the post immunization repertoire.

June et al. teach various production methods for generating antibodies, the immunogen may be a purified protein or alternatively may simple be a whole cell which expresses the surface protein of interest (see columns 21 and 22, especially column 22, lines 56-58). The reference also sets out the production of combinatorial antibodies (see column 26—27) from B-cell pools derived from immunized animals. The reference does not teach ligating the scFV-cDNA into a psi-negative retroviral Env expression vector.

It would have been obvious to one of ordinary skill in the art to make a cell specific retroviral using a single chain antibody following the steps of Dornburg. One having ordinary skill in the art at the time the invention was made would have been motivated to use whole cells for the immunization step in animals because the use of whole cells requires less preparation of the antigen. June et al. teaches that the use of whole cell as an immunogen in animals. One having ordinary sill in the art at the time would also recognize that injecting a whole cell in the

animal allows for the production of antibodies that recognize not only the cell surface receptors but also see the receptor in context of other cell surface molecules. Cholcer et al. teaches the production of an monoclonal antibody to a receptors using a membrane purified fraction this method required the addition step of the purification in addition the antibody producing cell then had to be fused in order to become immortalized. Novetony et al. teach that the step of producing the monoclonal antibody can be omitted and the RNA can be directly amplified from the IgG producing B-cells. One having ordinary skill in the art would have had a high expectation of success using the whole cell immunization step in order to obtain antibodies directed to a cell surface antigens. Therefore, the instant invention is obvious over Dornburg (U.S. Pat No. 5,869,331), Novotny et al. (in Molecular Biology and Biotechnology, 1995), Colcher et al. (Journal of the National Cancer Institute, 1990) and June et al. (U.S. Pat. No. 6,352,694 et al.).

***Conclusion***

Claims 9 and 19 are allowable, SEQ ID NO: 1 is free of the prior art of record.

Claims 1-8 and 20 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD
PATENT EXAMINER 10/20/03